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Resolution of hypercalcemia in primary hyperparathyroidism with vitamin D replacement

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ABSTRACT

Vitamin D deficiency is common in patients with primary hyperparathyroidism. We present a case of primary hyperparathyroidism with a positive parathyroid scan and history of nephrolithiasis. The patient had normal albumin and renal function but was vitamin D deficient. After treatment with vitamin D for 13 months, her parathyroid hormone values declined in parallel with the elevation in vitamin D. Although her total calcium normalized, her ionized calcium remained elevated throughout treatment. We believe vitamin D deficiency should be carefully monitored in primary hyperparathyroidism.

KEYWORDS Hyperparathyroidism; ionized calcium; parathyroid hormone; total calcium; vitamin D deficiency

Primary hyperparathyroidism (PHPT) has a population prevalence of 0.1% to 0.4%.[1] It is usually characterized by elevated serum calcium and elevated or unsuppressed serum parathyroid hormone (PTH) concentrations.[1] PHPT is also commonly associated with vitamin D deficiency. Vitamin D deficiency is associated with a more severe presentation of PHPT and occurs with a reported 91% to 100% incidence in PHPT patients.[2] Vitamin D supplementation has been proposed as a viable treatment option for PHPT despite concerns of further aggravating hypercalcemia.[3] Preliminary studies indicate that vitamin D replacement in mild PHPT reduces parathyroid levels significantly without exacerbating hypercalcemia.[3] There is no current consensus on managing vitamin D deficiency in PHPT.[4] We present a case of PHPT with a positive parathyroid scan and vitamin D deficiency. Replacing vitamin D was associated with normalization of serum calcium within 13 months.

CASE PRESENTATION

A 51-year-old Asian woman with known hypertension and a remote history of renal stones presented with hyperparathyroidism and vitamin D deficiency. She complained of fatigue and denied a family history of calcium issues. Her PTH was 86.8 pg/mL (normal value 14–72) and her 25-OH vitamin D level was 8.2 ng/mL (normal value 30–100). She was started on vitamin D2 50,000 IU/week and a daily multivitamin. Renal function was normal. Subsequent laboratory results revealed a 25-OH vitamin D of 17 ng/mL, an ionized calcium of 5.6 mg/dL (normal value 4.8–5.6), and a total calcium of 10.3 mg/dL (normal value 8.6–10.3) with an albumin of 3.8 g/dL. PTH levels were on the upper end of normal, measuring 62 pg/mL. The vitamin D regimen was switched to vitamin D3 5000 IU/day, and the patient was instructed to cease multivitamin intake.

At 8 months, her fatigue had lessened. Her total calcium and ionized calcium now were 11.3 mg/dL and 6.0 mg/dL (normal value 4.8–5.6), respectively. The urine calcium was 108 mg/24 h (normal value 100–300). Her vitamin D levels had improved *(Figure 1)*. She did admit to intermittent compliance with her vitamin D. Single photon emission computed tomography/computed tomography imaging revealed a right lower pole parathyroid adenoma. PHPT appeared likely given the history of kidney stones, positive parathyroid scan, elevated PTH values, and total calcium levels at the upper limit of normal. Magnesium and phosphorus measurements were normal. A dual energy x-ray absorptiometry bone density scan indicated a T score of –1.5 in the left femoral neck.

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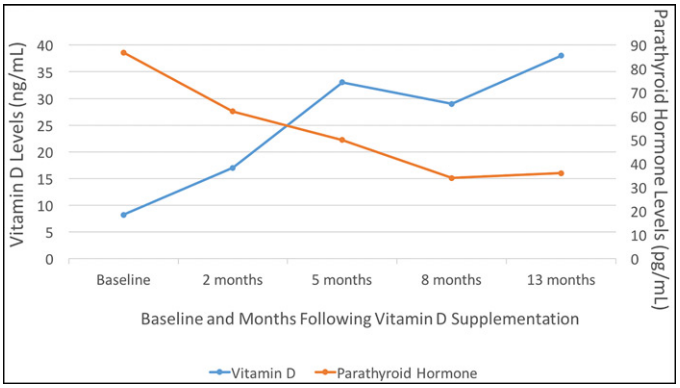

Figure 1. Vitamin D and parathyroid hormone levels over time.

The patient was maintained on 5000 IU of vitamin D3 daily and her progress was monitored. At follow up 13 months later, her total calcium levels had normalized (10.2 mg/dL) with an albumin of 4.1. The ionized calcium level remained elevated at 5.9 mg/dL. She declined parathyroidectomy.

DISCUSSION

We believe this to be the first reported case of normalization of total calcium following vitamin D replacement. Traditionally, parathyroidectomy procedures have been the definitive treatment for PHPT.[5] The decline in this patient's PTH level after treatment suggests that part of the PTH elevation was related to vitamin D deficiency (*Figure 1*). The urinary calcium, which is generally elevated in PHPT, is low in vitamin D deficiency and may have accounted for her relatively low urine calcium excretion.

Many physicians restrict vitamin D supplements for fear of aggravating hypercalcemia in PHPT.[3] However, studies suggest that vitamin D supplementation reduces PTH without adversely affecting serum calcium.[6] Other cases have reported on a small proportion of patients who experience slightly elevated calcium levels after vitamin D treatment. Due to patient variability, long-term clinical follow-up and longer duration of treatment are necessary.[2]

Guidelines for the management of PHPT are based on total serum calcium levels.[7] However, a small number of PHPT patients present with ionized calcium elevation without an elevated total calcium.[1] Ionized calcium is considered a more sensitive marker of PHPT severity. Our patient demonstrated persistent elevation in ionized calcium despite achieving a normal serum calcium. Despite arguments that ionized calcium levels may be unnecessarily sensitive, neglecting to test ionized calcium levels in a PHPT workup may lead to about 4% of patients with PHPT being missed.[7]

In our case, the patient experienced a temporary mild increase in total calcium that normalized along with her PTH levels after 13 months of vitamin D supplementation. Therefore, in patients presenting with PHPT and vitamin D deficiency, replacement of vitamin D may improve the total calcium but not the ionized calcium values. We believe current guidelines should be updated to include estimation of ionized calcium.

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